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Research Article

Analysis of factors among 30-day and 1-year mortality rates in patients with borderline stable-unstable intertrochanteric hip fracture

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ABSTRACT

Objective: This study aimed to evaluate the possible effects of surgical procedures on mortality and to identify the possible risk factors for mortality in the management of geriatric hip fractures.

Methods: A total of 191 patients (105 women and 86 men; mean age 82.26±9.681 [60-108] years) with AO/OTA 31A2.2 intertrochanteric fractures and treated with sliding hip screw, proximal femoral nail, or hemiarthroplasty were included in this retrospective cohort study. The treatment type was decided by the responsible surgeon according to the patients' pre-injury activity level, bone quality, and features of the fracture. Age, sex, type of fracture, type of surgery performed, American society of anesthesiology (ASA) grade, type of anesthesia, time to surgery, type of physical therapy, length of hospital stay, and number of comorbidities were documented. We evaluated the 30-day and 1-year mortality of patients treated with sliding hip screw (SHS), proximal femoral nail antirotation (PFN-A), or hemiarthroplasty and identified the possible risk factors for mortality.

Results: A total of 49 patients underwent SHS, 58 underwent PFN-A, and 84 underwent hemiarthroplasty. Of these, 2 patients with SHS, 2 with PFN-A, and 11 with hemiarthroplasty died within 30 days after surgery, whereas 7 patients with SHS, 15 with PFN-A, and 23 with hemiarthroplasty died 1 year after surgery. The 30-day and 1-year overall mortality rates were 7.9% and 23.6%, respectively. Both the 30-day and 1-year mortality risks were higher in patients undergoing hemiarthroplasty than in patients undergoing SHS ($p=0.068$ versus 0.058). The 30-day mortality was higher in patients receiving general anesthesia than in those receiving combined spinal and epidural anesthesia ($p=0.009$). The 1-year mortality risk was higher in patients with ASA grade 4 than in those with grade 1 and 2 ($p=0.045$). Advanced age ($p=0.022$) and male sex ($p=0.007$) were also found to be the risk factors for 1-year mortality.

Conclusion: We demonstrated that higher ASA grade, male sex, general anesthesia, and hemiarthroplasty procedures are associated with higher mortality rates in elderly patients with hip fractures. Thus, we highly recommend orthopedic surgeons to consider all these factors in the management of intertrochanteric hip fractures in the geriatric population.

Level of Evidence: Level IV, Prognostic Study

Introduction

Intertrochanteric fractures are relatively common in elderly patients (1). These are associated with high morbidity and mortality rates and result in temporary or permanent functional impairment and a decrease in the quality of life (2). Low energy and falls from standing height in patients with osteoporosis are the most common causes for intertrochanteric fractures (3). Hip fractures, especially seen in elderly patients, are associated with increased mortality rates (4, 5).

The aim of hip fracture treatment is to reduce pain and provide functional recovery with the lowest possible morbidity and mortality (6). Fixation of these fractures with an extramedullary sliding hip screw (SHS) and intramedullary proximal femoral nailing (PFN) or replacement by arthroplasty remains controversial (7, 8). Advanced age (9), male sex (10), presence of comorbid diseases (11), high American society of anesthesiologists (ASA) grade (12), and type of surgical procedure (6, 7) have been described as the predictive factors for mortality after a hip fracture. Furthermore, the effects of the duration of preoperative delay (13) on mortality remain debatable. A recent study mentioned the surgical procedure for hip fractures but did not report whether it had an impact on mortality (14). The postoperative 30-day (6) and 1-year (10) mortality rates are significantly high in geriatric patients with hip fractures. However, the role of predictive factors in mortality can change over time with improvements in surgical procedures, implants, and healthcare standards. These factors may also vary by region. We hypothesized that these high mortality rates might be related to the type of surgical procedure performed in the management of hip fractures in geriatric patients.

In this study, we aimed to evaluate the possible effects of surgical procedures on mortality and to identify the possible risk factors for 30-day and 1-year mortality in the management of AO/OTA31A2.2 intertrochanteric hip fractures in geriatric patients to guide the surgeons to better evaluate the high-risk patients and ultimately improve patient care.

Materials and Methods

This study was approved by the local ethics committee (Date: 11.07.2018, approval no. 2018.10.16). A total of 377 patients with hip fractures between January

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2010 and December 2017 were admitted to our clinic. Overall, 191 patients with an AO/OTA type 31A2.2 intertrochanteric hip fracture who underwent SHS (Figure 1), proximal femoral nail antirotation (PFN-A) (Figure 2), or hemiarthroplasty (Figure 3) were included in this retrospective study. Patients with intracapsular, subtrochanteric, or reverse oblique fractures; whose surgeries involved operations other than SHS, cephalomedullary nailing (CMN), or hemiarthroplasty; and those with time to surgery more than 15 days were excluded from the study. Patients with missing data relating to age, sex, length of hospital stay, ASA grade, or mortality status at 30-days and 1-year were also excluded. The treatment type was decided by the responsible surgeon according to patients' pre-injury activity level, bone quality, and features of the fracture. We evaluated AO/OTA type 31A2.2 fractures because they lie at the border of stable-unstable intertrochanteric fractures, and all 3 types of fixation devices have been widely used for their treatment. Moreover, AO type 31A2.2 was the most common type of intertrochanteric hip fractures among the geriatric patients who were admitted to our clinic.

We retrospectively documented age, sex, type of fracture, type of surgery performed, ASA grade, type of anesthesia, length of hospital stay, whether physical therapy was applied after surgery, number of comorbidities, and 30-day and 1-year mortality status of patients treated with SHS, PFN-A, or hemiarthroplasty. Injury mechanisms were categorized into fall from standing height, fall from a height, motor vehicle accident, battered, or unknown. The comorbidity data of these patients were identified using the International classification of diseases, 10th revision codes. Surgery-related data included type of surgical procedure performed, length of hospital stay, and status of physical therapy obtained from ENLIL system (ENLIL hospital information management system, version v2.19.46 20191118). Mortality records were obtained from the national population administration system.

The patients received a physical therapy protocol in the Department of Physical Therapy and Rehabilitation after surgery. The patients treated with SHS and CMN with an acceptable anatomical and stable reduction and all the patients treated with hemiarthroplasty were allowed weight bearing as much as they could tolerate on the first day after surgery. Postoperative physical therapy included transfer training, walking training, heel shift, isometric exercises of quadriceps and gluteal muscles, and active range of motion exercises of the hip and ankle joints. All the patients received their regularly used medications for their comorbid diseases. They also received daily enoxaparin sodium 4000 anti-Xa/0.4 mL subcutaneously and antiembolism knee-high inspection toe stockings.

Surgical techniques

The patients were positioned supine on the fracture table for SHS (Synthes®-Switzerland) and PFN-A (Synthes®-Switzerland). The ipsilateral arm was elevated in a sling, and the contralateral uninjured leg was placed on a leg holder for SHS. The "scissors" positioning was used forPFN-A. The ipsilateral hip was positioned in 10-15° adduction to the contralateral leg. Both the legs were placed in traction to prevent pelvic rotation. The injured hip was slightly flexed and adducted to allow nail entrance. The reduction was usually achieved by first pulling in the direction of the long axis of the leg to distract the fragments and regain length and then rotating internally. The reduction was checked intraoperatively in both the anteroposterior and lateral views with an image intensifier. The SHS plate was fixed to the femoral shaft with an appropriate number and size of plate holding the cortical and locking screws.

The patients were positioned in lateral decubitus with the ipsilateral arm in an arm sling for hemiarthroplasty. Padded cushions were placed under bony prominences to avoid excessive pressure. A preoperatively determined size (with the aid of radiographic templates) of cemented stem and a bipolar head (Stryker®, Omnifit®, Head/Neck Hip Stem, USA) were applied using a posterolateral approach.

Statistical analysis

Statistical Package for the Social Sciences version 23.0 (IBM SPSS Corp., Armonk, NY, USA) for Windows was used for the statistical anal-

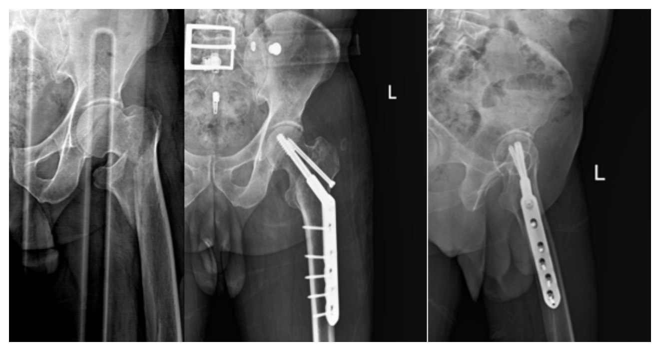

Figure 1. Preoperative and postoperative radiographs of a patient with a diagnosis of AO/OTA type 31A2.2 intertrochanteric fracture treated with sliding hip screw

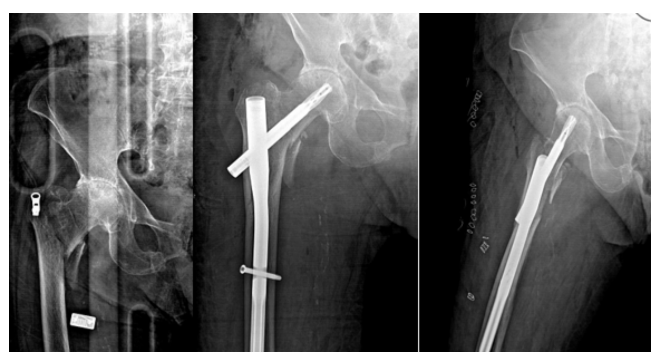

Figure 2. Preoperative and postoperative radiographs of a patient with a diagnosis of AO/OTA type 31-A2.2 intertrochanteric fracture treated with proximal femoral nail antirotation

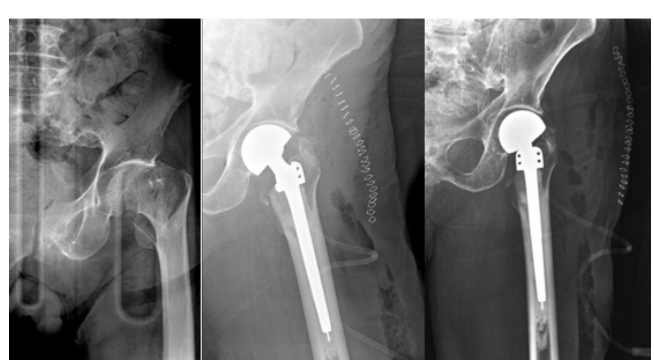

Figure 3. Preoperative and postoperative radiographs of a patient with a diagnosis of AO/OTA type 31-A2.2 intertrochanteric fracture treated with hemiarthroplasty

HIGHLIGHTS

- The 30-day mortality rate was highest in geriatric patients with AO/OTA type 31A2.2 hip fracture who underwent hemiarthroplasty. The 1-year mortality rate was lowest in geriatric patients with AO/OTA type 31A2.2 hip fracture who underwent SHS.
- General anesthesia had high risk of 30-day mortality. In addition, male gender and higher ASA grade had a high risk of 1-year mortality.
- There was no significant difference among surgical procedures in terms of mean age, ASA grade, comorbid disease, and complication rates.

ysis of the research data. In the descriptive statistics section, the categorical variables were presented as numbers and percentages and the continuous variables as mean±standard deviation and median (minimum-maximum). The suitability of the continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro-Wilk tests). The Mann–Whitney U test was used for comparative analysis between the 2 groups of data that did not fit the normal distribution. The Student's t test was used for the comparative analysis between 2 groups of normally distributed data. The Pearson chi-squared test was used for comparison of different categories, and if any expected frequency of <5 was obtained, the Fisher's exact test was used. The Kruskal-Wallis tests were conducted to compare the numerical variables of surgical treatment groups. Logistic regression analysis was performed for further analysis by modeling the factors that are possibly related to the 30-day and 1-year mortality, and the new models were obtained by gradually removing the variables until the most favorable model could be reached that could explain mortality within 30 days and 1 year. The level of statistical significance was accepted at $p<0.05$.

Results

The mean age of patients at the time of surgery was 82.26±9.68 (range, 60-108) years. The mean age of patients who were alive after 30 days from surgery was 82.08±9.85 years and that of those who died within 30 days after surgery was 84.4±7.34 years (p=0.325). The mean age of patients who were alive after 1 year from surgery was 81.27±9.29 years and that of those who died within 1 year after surgery was 85.47±8.13 years (p=0.011). A total of 105 patients were women, and 86 were men. Overall, 169 patients (88.5%) presented with a fall from a standing height as the mechanism of injury. A total of 49 patients underwent SHS, 58 underwent PFN-A, and 84 underwent hemiarthroplasty. Of these, 2 patients with SHS, 2 patients with PFN-A, and 11 patients with hemiarthroplasty died within 30 days of the surgery, whereas 7 patients with SHS, 15 patients with PFN-A, and 23 patients with hemiarthroplasty died within 1 year of surgery. Duo-analysis results of the possible risk factors with 30-day mortality and 1-year mortality are presented in Table 1.

Influence of treatment method

The overall 30-day mortality rate was 7.9%, and the distribution was as follows: SHS, 1.1%; PFN-A, 1.1%; and hemiarthroplasty, 5.7%. In addition, the 30-day mortality rates were 3.4% in patients who underwent PFN-A, 4.1% in patients who underwent SHS, and 13.1% in patients who underwent hemiarthroplasty (Table 2). The overall 1-year mortality rate was 23.6%, and the distribution was as follows: SHS, 3.7%; PFN-A, 7.9%; and hemiarthroplasty, 12%. The 1-year mortality rates were 14.3% in patients who underwent SHS, 25.9% in patients who underwent PFN-A, and 27.4% in patients who underwent hemiarthroplasty. In addition, the risk of 1-year mortality was 3.1 times higher in PFN-A and 3.2 times higher in hemiarthroplasty than that in SHS. Although the 30-day and 1-year mortality results were not statistically significant (p=0.058, p=0.068, respectively), these high rates are remarkable. There was no significant difference among the surgical procedures in terms of mean age, ASA grade, comorbid disease, and complication rates (p=0.723, p=0.092, p=0.179, and p=0.112, respectively). The detailed comparison of surgical procedures in terms of these risk factors is summarized in Table 3.

Table 1. Duo-analysis of possible risk factors and 30-day and 1-year mortality

	30-day mortality			1-year mortality		
	Dead n=15	Alive n=176	p	Dead n=45	Alive n=146	p
Sex, n=191 n (%)						
Male	9 (10.5)	77 (89.5)	0.225	26 (30.2)	77 (69.8)	0.049
Female	6 (5.7)	99 (94.3)		19 (18.1)	99 (81.9)	
Age, n=191						
Mean±SD	84.40±7.347	82.08±9.850	0.325	85.47±8.131	81.27±9.929	0.011
Type of anesthesia, n=191 n (%)						
Combine spinal and epidural	7 (5.1)	131 (94.9)	0.059	33 (23.9)	105 (76.1)	0.501
General Anesthesia	6 (18.75)	26 (81.25)		9 (28.1)	23 (71.9)	
Spinal	2 (9.5)	19 (90.5)		3 (14.3)	18 (85.7)	
Injury mechanism, n=191 n (%)						
Battered	0 (0)	1 (100)	<0.001	0 (0)	1 (100)	0.428
Fall from a height	1 (9.1)	10 (90.9)		3 (27.3)	8 (72.7)	
Fall from standing height	12 (7.1)	157 (92.9)		39 (23.1)	130 (76.9)	
Motor vehicle accident	0 (0)	7 (100)		1 (14.3)	6 (85.7)	
Unknown	5 (71.4)	2 (28.6)		2 (66.7)	1 (33.3)	
Side, n=191 n (%)						
Right	7 (7.7)	84 (92.3)	0.937	21 (23.1)	70 (76.9)	0.880
Left	8 (8)	92 (92)		24 (24)	76 (76)	
ASA grade, n=191 n (%)						
ASA 1+2	4 (7.4)	50 (92.6)	0.061	11 (20.4)	43 (79.6)	0.014
ASA 3	6 (5.4)	105 (94.6)		22 (19.8)	89 (80.2)	
ASA 4	5 (19.2)	21 (80.8)		12 (46.2)	14 (53.8)	
Physical therapy, n=191 n (%)						
Applied	1 (3.6)	27 (96.4)	0.362	3 (10.7)	25 (89.3)	0.083
Not applied	14 (8.6)	149 (91.4)		42 (25.8)	121 (74.2)	
Length of hospital stay, n=191						
Mean ±SD	8.27±4.008	8.39±5.140	0.953	9.13±6.465	8.14±4.530	0.252
Comorbidities, n=191 n (%)						
None	6 (10.9)	49 (89.1)	0.547	19 (34.5)	36 (65.5)	0.041
One	3 (5.4)	53 (94.6)		8 (14.3)	48 (85.7)	
Two or more	6 (7.5)	74 (92.5)		18 (22.5)	62 (77.5)	

ASA: American society of anesthesiologists

Influence of ASA and anesthesia type

In the logistic regression analysis, model 1 was found to be the ideal model to predict death in the first 30 days (Table 4). Model 1 had 1 variable that allowed us to predict death in 30 days. This variable was the type of anesthesia, and the probability of this variable predicting death was 13.4%. The risk of 30-day mortality was 3.97 times higher in patients receiving general anesthesia than in those receiving combined spinal-epidural anesthesia (p=0.046). Most of the patients were evaluated as ASA grade 3 (58.1%). The patients with ASA grade 4 had 4.47 times higher risk of death than those with ASA grade 1+2 within 1 year after surgery (p=0.041).

Table 2. Details of mortality rates according to surgical procedures

Surgical procedures, n=191 n (%)		SHS	PFN-A	Hemiarthroplasty	p
30-day mortality	Dead n=15	2 (4.1)	2 (3.5)	11 (13.1)	0.058
	Alive n=176	47 (95.9)	56 (96.5)	73 (86.9)	
1-year mortality	Dead n=45	7 (14.3)	15 (25.9)	61 (72.6)	0.203
	Alive n=146	42 (85.7)	43 (74.1)	23 (27.4)	

SHS, sliding hip screw; PFN-A, proximal femoral nailing antirotation

Table 3. Comparison of surgical procedures in terms of risk factors

	SHS n=49	PFN-A n=58	Hemiarthroplasty n=84	p
Age				
Mean±SD	80.78±10.57	82.21±9.51	83.17±9.26	
Median (Min-Max)	84 (60–96)	85 (61–101)	83.5 (61–108)	0.723
ASA grade				
ASA 1+2	21	16	17	
ASA 3	22	34	55	
ASA 4	6	8	12	0.092
Comorbid disease				
None	20	14	20	
1	10	21	27	
2 or more	19	23	37	0.179
Complications				
Infection	1	1	5	
Cut-through/Cut-out	4	6	0	
Dislocation	0	0	4	
Periprosthetic fracture	0	0	1	0.112

ASA, American society of anesthesiologists; SD, standard deviation

Influence of age and sex

In the logistic regression analysis, model 1 was the ideal model to predict death in 1 year (Table 4). Model 1 had 4 variables that allowed us to predict death in the first year. These variables were age, sex, ASA, and surgical procedure. The probability of these variables in predicting death is 25.7%. We found that increasing age increases the risk of 1-year mortality 1.06 times per year (p=0.038). Male patients had 2.91 times higher risk of death than female patients within 1 year after surgery (p=0.008). However, age and sex did not significantly affect the 30-day mortality (p=0.325, p=0.225, respectively).

Influence of comorbid diseases

Surprisingly, we found that patients without comorbid diseases had significantly higher risk of 1-year mortality than those with ≥2 comorbid diseases (p=0.041).

Discussion

Management of geriatric patients with intertrochanteric hip fractures has been a major health issue owing to their associated increased mortality, morbidity, and functional impact. The preferred treatment for hip fractures has been surgery owing to the increased mortality and morbidity rates associated with conservative treatment (15-17). The guidelines of the National Institute for Health and Care Excellence pointed out that the use of an intramedullary device in the treatment of AO type 31A1, 31A2, and 31A3 intertrochanteric hip fractures is associated with a high risk of postoperative complications (18). There was no significant difference between SHS and PFN-A in the performance of the implants in terms of fracture stability for AO/OTA 31A2 fractures (18, 19). However, there is an increased interest in CMN and hemiarthroplasty in the treatment of intertrochanteric fractures owing

Table 4. The logistic regression analysis for 30-day and 1-year mortality

	30-day			1-year		
	p	Odd ratio	95%CI	p	Odd ratio	95%CI
Age	0.873	1.006	0.935–1.082	0.038	1.056	1.003–1.112
Sex						
Female (ref)						
Male	0.105	2.869	0.801–10.276	0.010	2.818	1.277–6.218
Postoperative length of hospital stay	0.500	0.940	0.786–1.125	0.363	1.033	0.963–1.109
Preoperative length of hospital stay	0.979	1.003	0.774–1.301	0.427	0.923	0.758–1.125
Surgical procedure						
SHS (ref)						
PFN-A	0.768	1.377	0.165–11.517	0.059	2.957	0.960–9.108
Hemiarthroplasty	0.103	4.473	0.738–27.119	0.026	3.510	1.161–10.617
ASA grade						
ASA 1+2 (ref)						
ASA 3	0.925	0.919	0.158–5.344	0.698	0.795	0.249–2.537
ASA 4	0.121	6.019	0.624–58.072	0.041	4.473	1.065–18.786
Type of anesthesia						
Combine spinal and epidural (ref)						
General anesthesia	0.046	3.972	1.027–15.361	0.929	1.049	0.370–2.972
Spinal anesthesia	0.441	2.053	0.329–12.818	0.271	0.448	0.107–1.874
Physical therapy	0.492	2.267	0.219–23.419	0.348	1.943	0.485–7.790
Comorbidities						
2 or more (ref)						
1	0.759	0.767	0.140–4.189	0.209	0.489	0.160–1.493
None	0.180	3.422	0.567–20.641	0.074	2.715	0.909–8.107

ref, reference; SHS, sliding hip screw; PFN-A, proximal femoral nailing antirotation; ASA, American society of anesthesiologists; CI, confidence interval.

to their biomechanical advantages (9, 10). Hip fractures are reportedly associated with a 1-year mortality rate of 23.2%–30.8% (9, 20-22). In this study, the 30-day and 1-year mortality rates were 7.9% and 23.6%, respectively, which are comparable to the results of the previous literature. Our results revealed that the risk of 1-year mortality is higher for PFN-A and hemiarthroplasty than for SHS. Moreover, the risk of 30-day mortality is higher for patients undergoing hemiarthroplasty than for those undergoing PFN-A and SHS. However, the differences were not statistically significant. Whitehouse et al. reported an association between the use of intramedullary nail and higher 30-day mortality but not with the use of SHS, in AO/OTA 31A2 and AO/OTA 31A3 intertrochanteric fractures (6). They stated that the use of intramedullary nail would result in 1 more death for every 112 patients compared with SHS use. Our results also demonstrated a high risk of mortality with PFN-A even in the long term. Comparable to our study, Geiger et al. demonstrated that the 1-year mortality decreased in patients with AO/OTA 31A2 fracture who were treated with SHS (9). Similarly, Dobbs et al. reported a slightly higher 30-day mortality with arthroplasty than with open reduction and internal fixation methods (23). Both Geiger et al. (9) and Dobbs et al. (23) related the increase in mortality to increased ages of the patients receiving arthroplasty and their increased number of comorbid diseases. In contrast, there was no difference in the mean age between patients receiving hemiarthroplasty and those receiving other treatment methods in our study. There was also no significant difference among the surgical procedures in terms of ASA grade, comorbid disease, and complication rates. However, the mortality rate remained high in the patients undergoing arthroplasty. These results differed from those of previous literature. We consider that these increased mortality rates may be related to fat embolism and thromboembolism during the preparation of the femoral canal, cementation, and high volume of blood loss as a result of prolonged surgical time, rather than age difference. Ereth et al. reported that hip arthroplasty causes increased physiologic pulmonary dead space and high end-tidal to the arterial difference in the carbon dioxide partial pressures, and it has a negative effect on embolism, hemodynamics, and intrapulmonary shunting. Considering our results, we conclude that CMN is associated with life-threatening complications, probably because of intramedullary reaming and pressuring effects (24). We also considered that these increased mortality rates are causally related to implantation and techniques used for hemiarthroplasty. Thus, we recommend the surgeons to consider using SHS for AO type 31A2.2 fractures.

In contrast to the literature (11, 25), we could not demonstrate the effect of comorbid diseases on mortality. It could be owing to the fact that the patients with a higher number of associated comorbidities may keep their illnesses under control with frequent checkups. Furthermore, the patients who do not have any comorbid conditions or have only 1 comorbidity may have additional illnesses that have not yet been diagnosed or their illnesses may not be under control.

In the literature, the most commonly used anesthetic technique for hip fractures in geriatric patients is combined spinal and epidural anesthesia (26). We demonstrated that the 30-day mortality rate was 3.97 times higher for general anesthesia than for combined spinal and epidural anesthesia. The combined spinal and epidural anesthesia technique has minor effects on the cerebral function, avoids airway complications, and is a safe procedure under low blood pressure, thereby resulting in lower blood loss. In contrast to our study, other studies have reported that the anesthesia technique does not have a major impact on the 30-day mortality (26, 27). However, these studies focused on the increase in mortality because of the development of hypotension.

Several studies have reported that mortality rates are related to higher ASA grade (10, 11, 26). We demonstrated that patients with ASA grade 4 had a higher risk of 1-year mortality than patients with other ASA grades. There is also a controversial issue related to sex as a risk factor for increased mortality. Although the rate of hip fracture is higher in female patients (28), the 1-year mortality rate is higher in male patients (9, 10, 29). Multiple studies have correlated advanced age with increased 1-year mortality (9, 29), which is consistent with our findings. Geriatric male patients with higher ASA grade who had intertrochanteric hip fractures need to be evaluated carefully owing to their higher risk of mortality.

The limitations of this study include its retrospective nature, which increases the possibility that some episodes may have been missed. The sample size was small; however, we are confident that it is representative of the population of geriatric patients with an AO/OTA 31A2.2 intertrochanteric fracture of the hip. In addition, evaluation of postoperative complications of treatment methods could have been a significant predictor of mortality; however, this was not evaluated in this study. Finally, further studies are required to determine the association between mortality and parameters, such as tip-apex distance, reduction quality, head quadrants, and cut-out rates. Moreover, studies with larger participants are needed to support the effect of implant choice on mortality in geriatric patients with hip fractures.

In conclusion, we demonstrated that higher mortality rates in elderly patients with hip fractures are associated with several factors, such as high ASA grade, male sex, general anesthesia, and hemiarthroplasty procedures. Thus, we highly recommend the orthopedic surgeons to consider all these factors in the management of high-risk geriatric patients with intertrochanteric hip fractures to improve patient care.

Ethics Committee Approval: Ethics committee approval was received for this study from the Local Ethics Committee of Kırıkkale University (Date: 11.07.2018, approval no. 2018.10.16).

Informed Consent: N/A.

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